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CHOLESTEROL

Current Concepts for Clinicians

NATIONAL CHOLESTEROL EDUCATION PROGRAM

UPDATED VERSION

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

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Current Concepts for Clinicians

Updated Version

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The National Cholesterol Education Program
National Heart, Lung, and Blood Institute

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
National Institutes of Health

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I. Introduction

Coronary heart disease (CHD) remains the leading cause of death and disability in the United States despite recent declines in CHD morbidity and mortality. The prevention of CHD depends on the modification of three major risk factors: high blood cholesterol, cigarette smoking, and high blood pressure. In November 1985, the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH) launched the National Cholesterol Education Program (NCEP) in an effort to help decrease the incidence of illness and death from CHD in this country by reducing the prevalence of high blood cholesterol levels. The NCEP is one of three risk factor education programs of the NHLBI. The other two are the National High Blood Pressure Education Program and the NHLBI Smoking Education Program.

The effectiveness of lowering blood cholesterol as a means of reducing CHD risk was demonstrated conclusively in 1984 by the results of the Coronary Primary Prevention Trial (CPPT), which was supported and coordinated by NHLBI. Once the findings of the CPPT were known, a panel of experts was convened to participate in the NIH Consensus Development Conference on Lowering Blood Cholesterol to Prevent Heart Disease. The panel reviewed these results, along with a large body of evidence from pathological, animal, metabolic, epidemiological, and clinical studies.

This panel concluded that high blood cholesterol is indeed a major cause of CHD and that reducing high blood cholesterol, using dietary treatment and drug therapy, can prevent CHD development. Despite the findings from the spectrum of CHD research, many facts are inadequately appreciated by many health professionals and the public.

For example, the results of the NHLBI's Cholesterol Awareness Survey of physicians conducted in 1983, prior to the release of the CPPT results, and again in 1986 showed that the proportion of physicians who believed that lowering high blood cholesterol would have a large effect in preventing CHD improved from 39 percent in 1983 to 64 percent in 1986. Yet, thirty-six percent of physicians remained to be fully convinced. In 1986, even though more physicians were initiating dietary treatment for their patients at levels closer to the Consensus Development Conference recommendations, only about 50 percent of physicians were initiating dietary treatment for their patients in the top 25 percent of the blood cholesterol distribution. In terms of initiating drug therapy for appropriate patients in the top 10 percent of the cholesterol distribution as recommended by the Consensus Conference, 36 percent of physicians never or virtually never used drugs to treat high blood cholesterol. These results indicate that while there has been a significant change in cholesterol-related attitudes and practices since 1983, there is still clearly a need for information about high blood cholesterol management.

To meet the needs of professionals and the public, the NCEP provides cholesterol information in four program areas: professional and patient education, public education, worksite programs, and school-based education. The leadership body of the NCEP is the Coordinating Committee, which comprises representatives from more than 35 health-related organizations and associations involved in health and cholesterol education. Some of the major organizations represented on the committee include the American Heart Association, American Medical Association, and the American College of Cardiology. The Committee meets three times a year to review educational strategies and define activities that will further the aims of the program. In addition, the Committee convenes expert panels to address specific needs of the program. To date, the following three expert panels have been convened; the Adult Treatment Panel, the Laboratory Standardization Panel, and the Population-Based Panel. Another group of experts will soon be convened to focus on children and adolescents with high blood cholesterol levels.

The Adult Treatment Panel (ATP) was charged with developing a report providing specific guidelines for the detection, evaluation, and treatment of high blood cholesterol levels in adults. This CME monograph is based primarily on the panel's October 1987 report.

The panel addressed persons 20 years of age and above. Data from the National Health and Nutrition Examination Survey reveal that over 25 percent of the adult U.S. population (20 years of age and older) or more than 40 million Americans have high blood cholesterol levels. More than half of all adult Americans have a blood cholesterol level that is higher than desirable.

The ATP report makes several recommendations that further refine previous cholesterol management guidelines. For example, the report defines high blood cholesterol as a total cholesterol of 240 mg/dl or greater, and recommends that an average of repeat measurements be used for classifying patients' blood cholesterol levels. Total blood cholesterol levels are the basis for initial patient classification. Low-density lipoprotein (LDL) cholesterol levels, however, are recommended as the basis for treatment decisions. The report establishes specific LDL-cholesterol cutpoints (or treatment-initiation levels) and goals for dietary and drug regimens. It emphasizes the importance of viewing the risk associated with blood cholesterol levels in the context of other CHD risk factors. The recommended two-step dietary treatment approach progressively reduces the intake of saturated fat and dietary cholesterol. In addition, the report outlines the use of agents currently available for drug therapy, for instances when dietary therapy alone proves insufficient.

This monograph, while not comprehensive, presents current perspectives and information from the NCEP panel and other authorities in the field of cholesterol research and management. The subjects covered include: coronary heart disease: evidence for the role of blood cholesterol; lipoprotein metabolism and hypercholesterolemia; classification of patients by total and LDL-cholesterol levels; testing for high blood cholesterol; dietary treatment; drug treatment; and the importance of a multidisciplinary team approach. These topics correspond to information abstracted from the ATP report and other scientific papers.

II. Coronary Heart Disease: Evidence for the Role of Blood Cholesterol

Although CHD mortality rates have decreased over the past 20 years, this disease is still responsible for more than one-half million deaths in the United States each year, which is more than the deaths from all forms of cancer combined. It is estimated that CHD, directly and indirectly, costs the United States more than $100 billion a year.

Over the years, scientific investigation has focused on the need to establish the causes of CHD and, ultimately, the means to prevent it. The primary cause of CHD is atherosclerosis, a type of arteriosclerosis that affects large arteries. Atherosclerosis is a progressive disease that narrows the channels of the coronary arteries and is responsible for most heart attacks. A large body of scientific evidence has been collected from epidemiological, genetic, clinical, metabolic, experimental animal, pathological, and intervention studies identifying high blood cholesterol levels as a major risk factor for CHD. Such studies include experiments in animals which show that many species develop atherosclerosis when fed diets

that raise their blood cholesterol level. In these animals, atherosclerosis regresses when blood cholesterol levels are lowered.

Human studies have shown that lowering high blood cholesterol levels (particularly high levels of low-density lipoproteins)[1] reduces the risk of CHD. A recent study has shown that lowering blood cholesterol levels can slow down the atherosclerotic process and even lead to regression of existing lesions. While cigarette smoking and high blood pressure have been recognized as two other major modifiable risk factors in the development of CHD, now there is little doubt that elevated blood lipids play an important and perhaps facilitatory role in the development of atherosclerosis and, therefore, CHD.

Although many studies demonstrate the relationship between blood cholesterol and CHD, the following studies provide some of the most important evidence available on that relationship.

In 1948, the Framingham Study investigators began following more than 5,000 men and women in Framingham, Massachusetts. The majority were free of clinical evidence of heart disease when they entered the study and have since been regularly monitored for the development of CHD. This major prospective study is credited with establishing the risk factor concept for CHD. The data obtained from these men and women indicated a strong relationship between total and low-density lipoprotein (LDL) cholesterol levels and CHD, as well as a protective relationship between high-density lipoprotein (HDL) cholesterol levels and CHD. In addition, the Framingham data indicated that the impact of high blood cholesterol is augmented by other risk factors, showing CHD to be a multifactorial disease.

Survey and research data gathered over the past 30 years have shown that the severity of CHD increases as blood cholesterol levels rise. For example, the data from the Framingham Study suggested that people with blood cholesterol levels above 200 mg/dl have an increased risk of developing CHD.

Data made available in 1982 from the Multiple Risk Factor Intervention Trial (MRFIT) support the Framingham data but go a step further. Over 350,000 men were screened for the trial (70 times the number of people in the Framingham Study) and were followed to track the causes of death. The findings as shown in Figure 1 suggest that even cholesterol levels below 200 mg/dl may carry some increased risk of CHD.

The effects of interventions, whether diet and/or drugs, on lowering total blood cholesterol levels have been demonstrated in more than a dozen trials. These studies have provided encouraging evidence that CHD rates can be reduced by lowering total blood cholesterol levels. However, conclusive evidence that reducing high cholesterol levels decreases the rate of heart attacks and deaths caused by heart attacks was provided by the Coronary Primary Prevention Trial (CPPT). The CPPT was a double-blind study involving more than 3,800 middle-aged men, all free of CHD at entry but at high risk for CHD because their blood cholesterol levels were greater than 265 mg/dl (greater than the 95th percentile). Each participant was prescribed either cholestyramine resin, a bile acid sequestrant, or an equivalent amount of placebo. All were on a moderate cholesterol-lowering diet, and all were followed for 7 to 10 years.

In the drug-treated group there was an average decrease in total plasma cholesterol of 13.4 percent and an average decrease in LDL-cholesterol of 20.3 percent. These reductions were 8.5 percent greater for total cholesterol and 12.6 percent greater for LDL-cholesterol than the reductions in the placebo-treated group. In the drug-treated group, a 9-percent decrease in total cholesterol was associated with a 19-percent reduction in definite CHD deaths and/or nonfatal myocardial infarction. The findings indicated that with a 25-percent drop in blood cholesterol levels there was a 49-percent reduction in heart attacks and heart attack deaths.

The CPPT provided conclusive evidence that high blood cholesterol levels play a causal role in the development of CHD. Consistent with the Framingham data and other studies, the CPPT showed that for each 1-percent reduction in total blood cholesterol there was an approximate 2-percent reduction in the incidence of fatal and nonfatal heart attacks in men with high blood cholesterol levels. Furthermore, the

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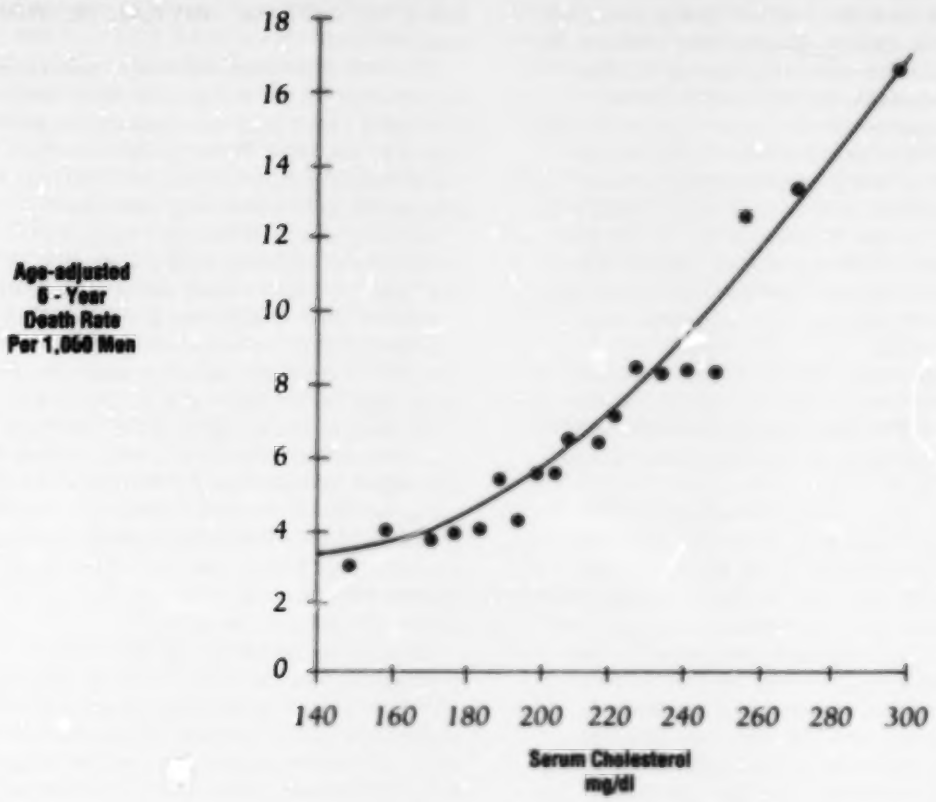
1 The next section of this monograph describes lipoprotein fractions, including low-density lipoprotein and high-density lipoprotein, in detail.

Figure 1:



Key Points:

(1) The risk increases steadily, and particularly above 200 mg/dl.

(2) The magnitude of the increased risk is large—fourfold in the top 10% as compared to the bottom 10%.

CPPT demonstrated that by reducing total blood cholesterol–and specifically lowering LDL-cholesterol–CHD morbidity and mortality could be reduced.

In 1987, results of the Cholesterol-Lowering Atherosclerosis Study (CLAS) provided additional evidence of the benefit of treatment to reduce blood cholesterol. The study population comprised 188 men ages 40 to 59 (nonsmokers or ex-smokers) whose entry blood cholesterol was between 185 and 350 mg/dl. All patients had had a previous coronary artery bypass graft because of severe disease of their native coronary arteries.

The aggressively treated group received a combination of diet, colestipol, and nicotinic acid to produce marked reductions in total cholesterol (down 26 percent) and LDL-cholesterol (down 43 percent) and a marked increase in HDL-cholesterol (up 37 percent). The control group received diet and placebos which resulted in a total cholesterol reduction of 4 percent, an LDL-cholesterol reduction of 5 percent, and an HDL-cholesterol increase of 2 percent. The treatment improved the profile of the atherosclerotic lesions in the grafts of the native vessels as assessed by angiography. In the placebo group, 61 percent had various degrees of progression of their lesions compared with 39 percent of the drug-treated group. Sixteen percent of the drug-treated group showed evidence of regression compared with only 2 percent of the placebo group.

Recent findings from the Helsinki Heart Study, a 5-year double-blind trial of 4,081 asymptomatic middle-aged men with primary dyslipidemia, provided additional evidence of the role of lipid modification in preventing CHD. The group of men receiving 600 mg of gemfibrozil twice daily had moderate reductions in serum levels of total and LDL-cholesterol and triglycerides, and an increase in HDL-cholesterol. The placebo group had minimal lipid changes. The gemfibrozil group experienced a 34-percent reduction in the incidence of CHD when compared to the control group. These findings warrant further analysis in order to assess fully the implications of the trial, but the findings are generally in accord with the CPPT study, which also demonstrated that lowering cholesterol levels significantly decreases the incidence of major coronary events.

III. Lipoprotein Metabolism and Hypercholesterolemia

By the early 1970's, epidemiological studies had established that high blood levels of total and LDL-cholesterol increase the risk of CHD. The Nobel Prize-winning research of Drs. Michael Brown and Joseph Goldstein at the University of Texas demonstrated that a defect in LDL receptor activity is linked with high blood cholesterol levels. Their work has underscored the importance of understanding the role of lipoprotein fractions and their relation to CHD risk.

Cholesterol is insoluble in plasma; therefore, it is packaged into lipoprotein complexes for transport. These complexes are composed of a variety of lipids, including triglycerides, phospholipids, free and esterified cholesterol, and specific proteins known as apoproteins. Different lipoprotein fractions contain varying amounts of lipids and proteins, and consequently vary in and can be identified by their density. They include chylomicrons, very low-density lipoproteins (VLDL), intermediate-density lipoproteins (IDL), LDL, and HDL. About 50 to 70 percent of the circulating cholesterol in the blood normally is carried in LDL, the most atherogenic of the lipoproteins. In contrast, about 25 percent of the total cholesterol is found in HDL, while VLDL carries most of the plasma triglycerides and only about 10 to 15 percent of the total cholesterol. As the Framingham investigators found, the higher the levels of LDL, the higher the risk of developing CHD. Conversely, the higher the level of HDL, the lower the risk of CHD.

The relationship between these fractions and their role in the potential development of CHD can be seen by reviewing the two pathways of the lipoprotein transport system: the *exogenous* and the *endogenous* pathways.

The exogenous pathway begins in the intestine where dietary lipids are digested. Products of lipid digestion are assembled in the intestinal wall into chylomicrons. The chylomicrons are then transported into the peripheral circulation through the thoracic-lymphatic system. In muscle and adipose tissue capillaries, the enzyme lipoprotein lipase hydrolyzes triglycerides. The resultant fatty acids are either stored in adipose tissue or used by muscles for energy, while the remaining components are rearranged into cholesterol-rich remnant particles and removed from the circulation by the liver. Cholesterol from the remnants is excreted into the intestine primarily as bile acids or reassembled with triglycerides in the liver into VLDL and released into the circulation.

At this point, the endogenous pathway begins. Like chylomicrons, when the triglyceride-rich VLDL reaches adipose or muscle tissue it loses most of its triglycerides through the action of lipoprotein lipase, thereby leaving cholesterol-rich IDL. Some IDL is removed

from the circulation by LDL receptors in the liver. Other IDL is converted into LDL. Most of the LDL binds to the LDL receptors on the liver or to LDL receptors on extrahepatic cells and is removed from the circulation.

LDL receptors play a critical role in the regulation of blood cholesterol levels. The number of receptors present on a cell surface depends on the cell's need for cholesterol. When there is an oversupply of cholesterol available to the cell or when the cell's demand for cholesterol is low, the manufacture of receptors is inhibited. This results in a reduced rate of LDL uptake, an accumulation of excess cholesterol in the circulation and an acceleration of the atherosclerotic process. The mechanism by which increased plasma levels of LDL are thought to promote atherogenesis is described by Drs. Brown and Goldstein. They note that LDL particles and blood platelets penetrate damaged arterial endothelium. In addition, smooth muscle cells from the layer below the endothelium multiply and migrate into the damaged area. Simultaneously, circulating white blood cells are activated to become macrophages that, along with the smooth muscle cells, ingest and degrade LDL to become foam cells. In the presence of high blood levels of LDL, cholesterol from the LDL accumulates in and around the foam cells. This accumulation of cells, cholesterol, and other debris creates atheromas. As atheromas continue to enlarge, they narrow the arterial opening and eventually lead to occlusion of the artery.

HDL, which is formed in the liver, appears to pick up cholesterol from extrahepatic cells, esterifies it, and carries it back to the liver. This process is known as "reverse cholesterol transport." Esterified cholesterol also may be transferred from HDL to VLDL and to LDL and transported back to the liver. The capacity of HDL to remove cholesterol from extrahepatic tissue may explain its protective role in relation to CHD risk.

An elevated level of LDL in the plasma, which is associated with increased CHD risk, results either from its overproduction or from a defect in its removal. For example, in familial hypercholesterolemia (FH), fewer than normal LDL receptors are present on cell surfaces or the functioning of those receptors synthesized is impaired. Consequently, less LDL enters cells, more LDL remains in circulation, and plasma LDL increases. Since less cholesterol enters the cell, cholesterol synthesis increases. FH heterozygotes inherit one mutant gene, resulting in one-half the normal number of LDL receptors and in LDL levels about twice the normal level. FH homozygotes inherit two mutant genes, resulting in LDL levels four to six times higher than normal.

Only about 1 in 500 people is an FH heterozygote, and 1 in 1,000,000 is an FH homozygote. This accounts for less than 2 percent of all cases of primary hypercholesterolemia. The majority of people with high blood cholesterol do not appear to have this genetic abnormality. Dr. Scott Grundy of the Center for Human Nutrition at the University of Texas cautions that although a genetic insufficiency of functional LDL receptors is a cause of high blood cholesterol, for a larger number of people diet is a significant factor. Several studies indicate that diets high in both saturated fat and cholesterol lead to high LDL cholesterol levels, promoting the accumulation of cholesterol in liver cells. This accumulation in turn suppresses the manufacture of LDL receptors and leads to diminished uptake of LDL from the blood.

IV. The Adult Treatment Panel's Classification of Patients by Total and LDL-Cholesterol Levels

In order for physicians to have practical guidelines to use in measuring and reducing high blood cholesterol levels, the Adult Treatment Panel recommended a classification system based on total cholesterol and LDL-cholesterol measurements to detect, evaluate, and treat patients. The classifications, which are based on epidemiological and clinical considerations, use total cholesterol measurements initially to identify individuals with elevated levels, and then LDL-cholesterol levels to guide treatment decisions regarding patients at risk. The cutpoints recommended are uniform for all men and women 20 years of age and older.

Initial Classification by Total Cholesterol

The classification system begins with measurement of the total cholesterol level. Serum is most frequently used for this measurement. The cutpoints for initial classification based on total cholesterol appear in Figure 2. The panel recommended that patients with a *desirable blood cholesterol* level (<200 mg/dl) be given advice and educational materials on current dietary recommendations for the general population and be advised to have another serum cholesterol test within 5 years. As with all patients, these individuals should also have been evaluated for other CHD risk factors. The ATP defined "other CHD risk factors" to include male sex, family history of CHD (definite myocardial infarction or sudden death before age 55 in a parent or sibling), cigarette smoking (currently smokes more than 10 cigarettes per day), hypertension, low HDL-cholesterol concentration (below 35 mg/dl confirmed by repeat measurement),* diabetes mellitus, history of definite cerebrovascular or occlusive peripheral vascular disease, and severe obesity (>30 percent overweight).

Patients with confirmed *borderline-high blood cholesterol* levels (200 to 239 mg/dl) who are free of CHD and have less than two other factors that increase CHD risk should be given dietary education designed to lower serum cholesterol level and should be followed up annually. However, those individuals in the 200 to 239 mg/dl range who have definite CHD or two other CHD risk factors should have a lipoprotein profile analysis and their LDL-cholesterol level determined. The LDL level provides a more precise estimate of risk.

All patients with *high blood cholesterol* levels (240 mg/dl or greater) should be tested for the serum level of LDL-cholesterol, which is used as the basis for treatment decisions.

Because the relationship between serum cholesterol level and CHD is a continuous and steadily increasing one, these cutpoints are necessarily somewhat arbitrary. However, this is also true of other risk factors, such as blood pressure, and the success of basing clinical decisions on whether a patient is classified as hypertensive indicates the value of establishing cutpoints for clinical decisions. The 240 mg/dl cutpoint for total serum cholesterol corresponds approximately to the 75th percentile for the adult U.S. population; it is a level at which CHD risk is almost double that at 200 mg/dl and is rising steeply. Patients with cholesterol levels at or above this cutpoint have sufficiently high risk to warrant more detailed evaluation and possible treatment. Survey data show that about 25 percent of the U.S. adult population, or about 40 million people ages 20 and above, fall into this category.

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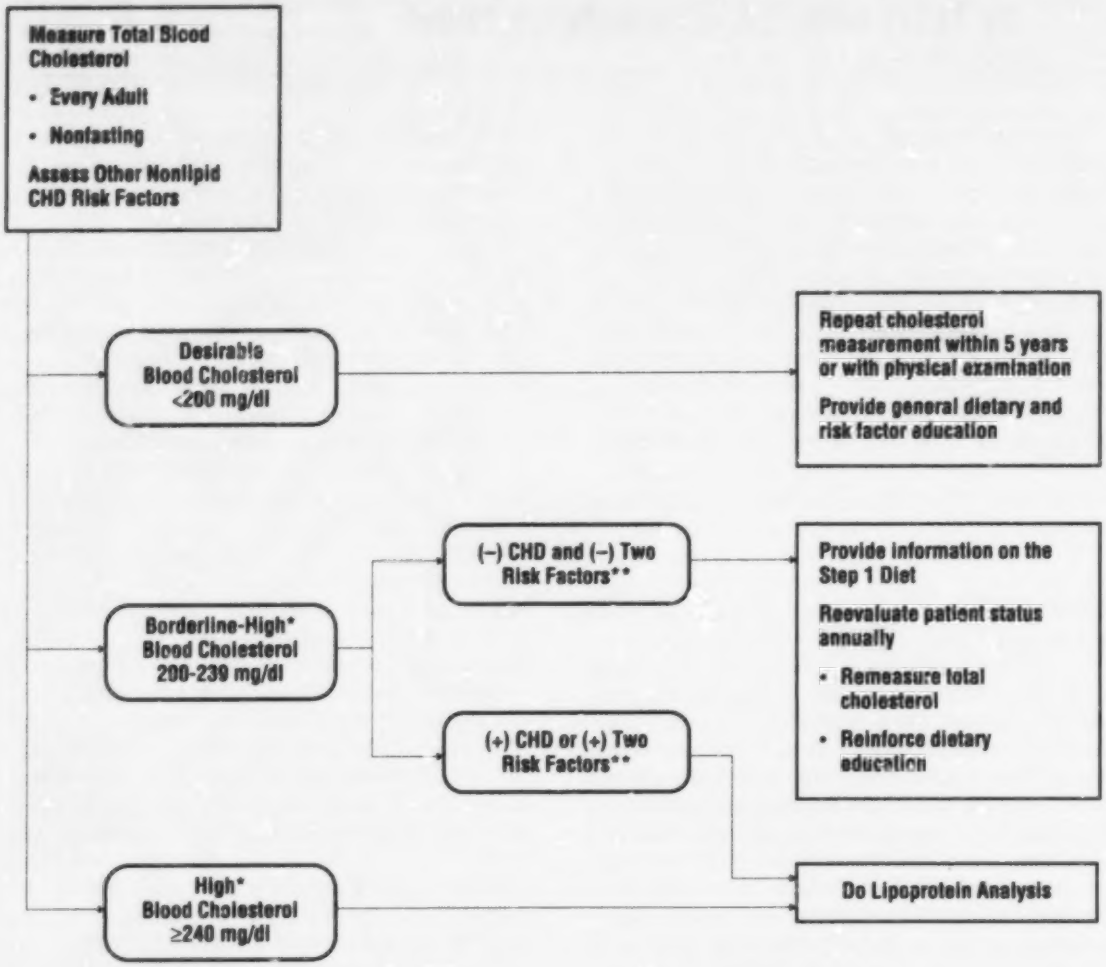
* Not determined at initial screening.

Figure 2: Initial Classification Based on Total Cholesterol


Measure Total Blood Cholesterol
• Every Adult
• Nonfasting
Assess Other Nonlipid CHD Risk Factors
Desirable Blood Cholesterol <200 mg/dl
Repeat cholesterol measurement within 5 years or with physical examination
Provide general dietary and risk factor education
Borderline-High* Blood Cholesterol 200-239 mg/dl
(–) CHD and (–) Two Risk Factors**
(+) CHD or (+) Two Risk Factors**
Provide information on the Step 1 Diet
Reevaluate patient status annually
• Remeasure total cholesterol
• Reinforce dietary education
High* Blood Cholesterol ≥240 mg/dl
Do Lipoprotein Analysis

* Must be confirmed by repeat measurement; use average value
** One of which can be male sex

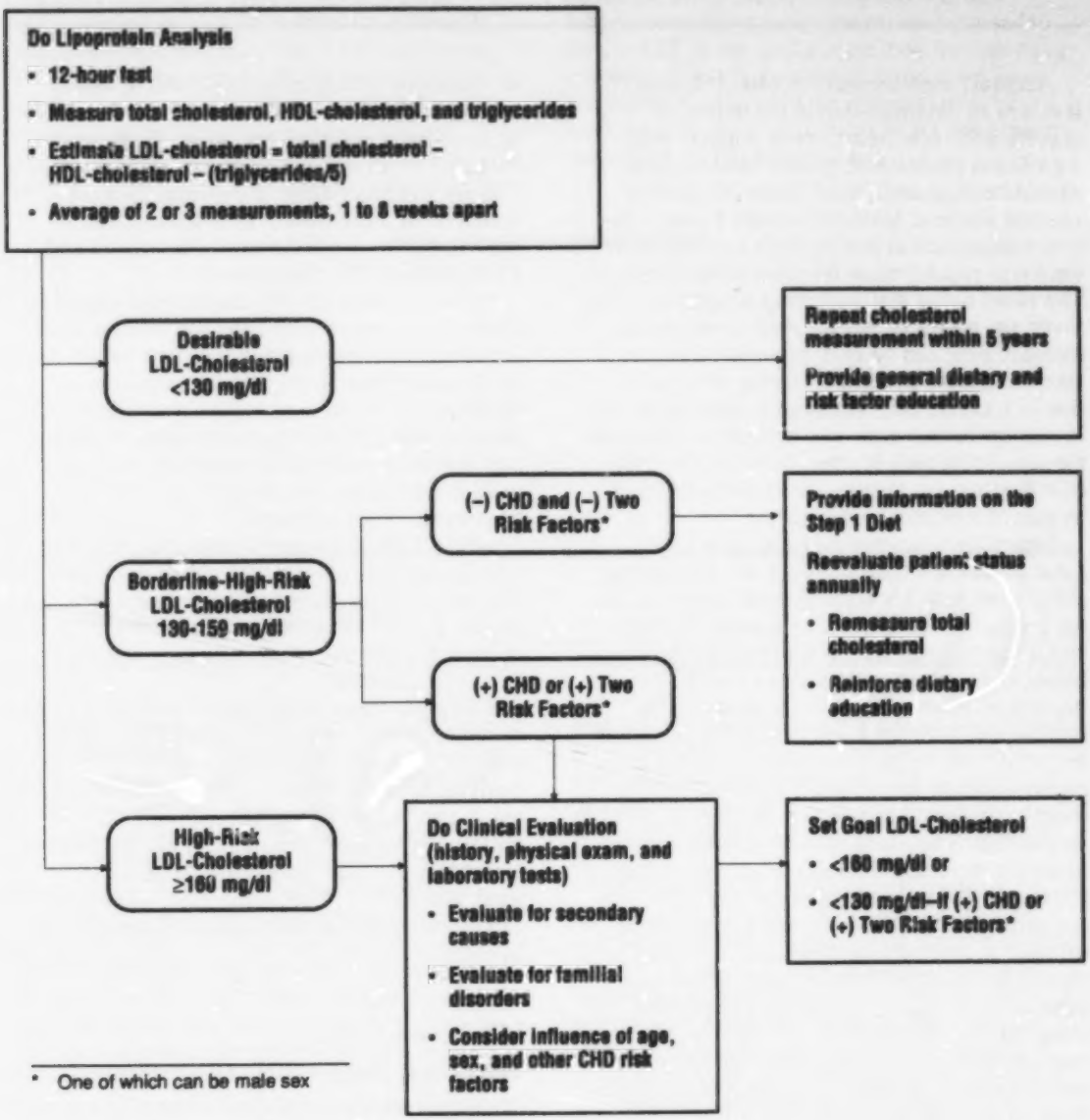
Subsequent Classification by LDL-Cholesterol

The panel classified LDL-cholesterol levels and the corresponding action scheme as shown in Figure 3.

Patients with *desirable LDL-cholesterol* (<130 mg/dl) are treated in the same way as those with desirable total cholesterol levels (<200 mg/dl), i.e., they should be given general dietary and risk reduction educational materials and tested again within 5 years.

Those with *borderline-high-risk LDL-cholesterol* (130 to 159 mg/dl) who are free of CHD and have less than two risk factors for CHD (similar to persons with borderline-high total cholesterol who are similarly free of CHD and have less than two CHD risk factors) should receive information about and be advised to follow a fat-modified diet and should be reevaluated annually. Patients with borderline high-risk LDL-cholesterol who also have definite CHD or two other CHD risk factors should be evaluated clinically and enter a

Figure 3: Classification Based on LDL-Cholesterol


Do Lipoprotein Analysis
• 12-hour fast
• Measure total cholesterol, HDL-cholesterol, and triglycerides
• Estimate LDL-cholesterol = total cholesterol – HDL-cholesterol – (triglycerides/5)
• Average of 2 or 3 measurements, 1 to 8 weeks apart
Desirable LDL-Cholesterol <130 mg/dl
Repeat cholesterol measurement within 5 years
Provide general dietary and risk factor education
Borderline-High-Risk LDL-Cholesterol 130-159 mg/dl
(–) CHD and (–) Two Risk Factors*
(+) CHD or (+) Two Risk Factors*
Provide information on the Step 1 Diet
Reevaluate patient status annually
• Remeasure total cholesterol
• Reinforce dietary education
High-Risk LDL-Cholesterol ≥160 mg/dl
Do Clinical Evaluation (history, physical exam, and laboratory tests)
• Evaluate for secondary causes
• Evaluate for familial disorders
• Consider influence of age, sex, and other CHD risk factors
Set Goal LDL-Cholesterol
• <160 mg/dl or
• <130 mg/dl–If (+) CHD or (+) Two Risk Factors*
* One of which can be male sex

blood cholesterol-lowering treatment program (see pages 11-21). Patients in the *high-risk LDL-cholesterol* group also should undergo a thorough clinical evaluation and then be treated. The goals of clinical evaluation are to determine whether a high LDL-cholesterol level is caused by another disease, by a drug, or by a genetic disorder, and to ensure that the patient is fully characterized with regard to factors that affect treatment decisions, including age, sex, and the presence of other CHD risk factors.

V. Testing for High Blood Cholesterol

Accurate measurement of blood cholesterol levels is an essential step in the detection, classification and treatment of patients with high blood cholesterol. Serum total cholesterol should be measured in all adults 20 years of age and above at least once every 5 years. Patients diagnosed as having high blood cholesterol will require more frequent measurements. The panel noted that screening programs which invite the public to receive their cholesterol measurement can be used provided that care is taken to ensure that the screening determination is accurate and that there is appropriate followup for further tests and treatment. However, the usual approach is expected to be through case finding, i.e., testing the cholesterol level as part of a medical examination.

Serum total cholesterol levels can be measured at any time of day in the nonfasting state, since total cholesterol concentrations do not change appreciably after a meal. Patients should be following their ordinary eating habits and in their usual state of health. To prevent an effect of posture or stasis on the cholesterol determination, venipuncture should be carried out on patients who have been in the sitting position for at least 5 minutes, and the tourniquet should be used for as brief a period as possible. The blood may be collected either as serum (no anticoagulant) or as plasma (in EDTA). If blood is obtained without anticoagulant, it should be allowed to clot for 30 minutes at room temperature, and the clot should be detached from the wall of the tube prior to centrifuging. Rapid capillary blood (fingerstick) methodology for cholesterol measurement is currently under development and evaluation. Should this methodology prove reliable, it could be suitable for initial total cholesterol determinations.

Patients with a serum cholesterol of 200 mg/dl or greater should have a repeat measurement in 1 to 8 weeks in order to confirm the value. If the total cholesterol level is within 30 mg/dl of the first result, the average of the two values can be used to guide subsequent decisions; otherwise, a third test should be obtained within another 1 to 8 weeks and the average of the three values used. Getting more than one cholesterol measurement at the outset of treatment is extremely important to assess the patient's serum cholesterol status accurately, because cholesterol levels can fluctuate considerably from day to day in a given individual. The standard deviation of repeated measurements in an individual over time has been reported as 18 mg/dl for total cholesterol and 15 mg/dl for LDL-cholesterol.

Measurements of LDL-cholesterol should be made 1 to 8 weeks apart, and the average used for clinical decisions unless the two values differ by more than 30 mg/dl (in which case a third test is carried out, and the average of all three is used). Repeat measurements are important due to the individual variability from day to day and the need to establish an accurate baseline in order to design the best treatment program. LDL-cholesterol determinations can also be carried out on either serum or plasma, provided that, as with total cholesterol measurements, plasma values are multiplied by 1.03 to correct them to the serum cutpoints specified in this monograph.

The LDL-cholesterol level is estimated from measurements of the levels of total cholesterol, total triglycerides, and HDL-cholesterol. If the triglyceride value is below 400 mg/dl, then this value can be divided by 5 to estimate the VLDL-cholesterol level. Since total cholesterol is the sum of LDL-cholesterol, HDL-cholesterol, and VLDL-cholesterol, LDL-cholesterol can be calculated as follows (all quantities are in mg/dl):

LDL–Cholesterol=

Total Cholesterol – HDL–Cholesterol –

(Triglyceride/5)

If triglyceride is above 400 mg/dl, the above formula is less accurate and ultracentrifugation in a specialized laboratory can be used to give a more accurate LDL-cholesterol level. Since LDL-cholesterol is estimated from measurements of other lipids including triglyceride, blood samples should be collected from patients who have fasted for at least 12 hours (except for water or black coffee).

The choice of laboratory is an important issue because there is considerable variability in the accuracy with which laboratories measure cholesterol. The physician should seek a laboratory that participates in a suitable standardization program. The National Bureau of Standards, the Centers for Disease Control, and the College of American Pathologists provide certified reference materials to improve accuracy and precision of cholesterol measurements. The Laboratory Standardization Panel of the NCEP is developing plans for improved national cholesterol standardization as well as reviewing the new fingerstick testing methods. The panel recommends that all laboratories adopt the cutpoints recommended by the ATP as the uniform method for reporting cholesterol levels, to eliminate the wide interlaboratory variation in the interpretation of cholesterol values. (See page 22 for additional laboratory recommendations.)

VI. Dietary Treatment

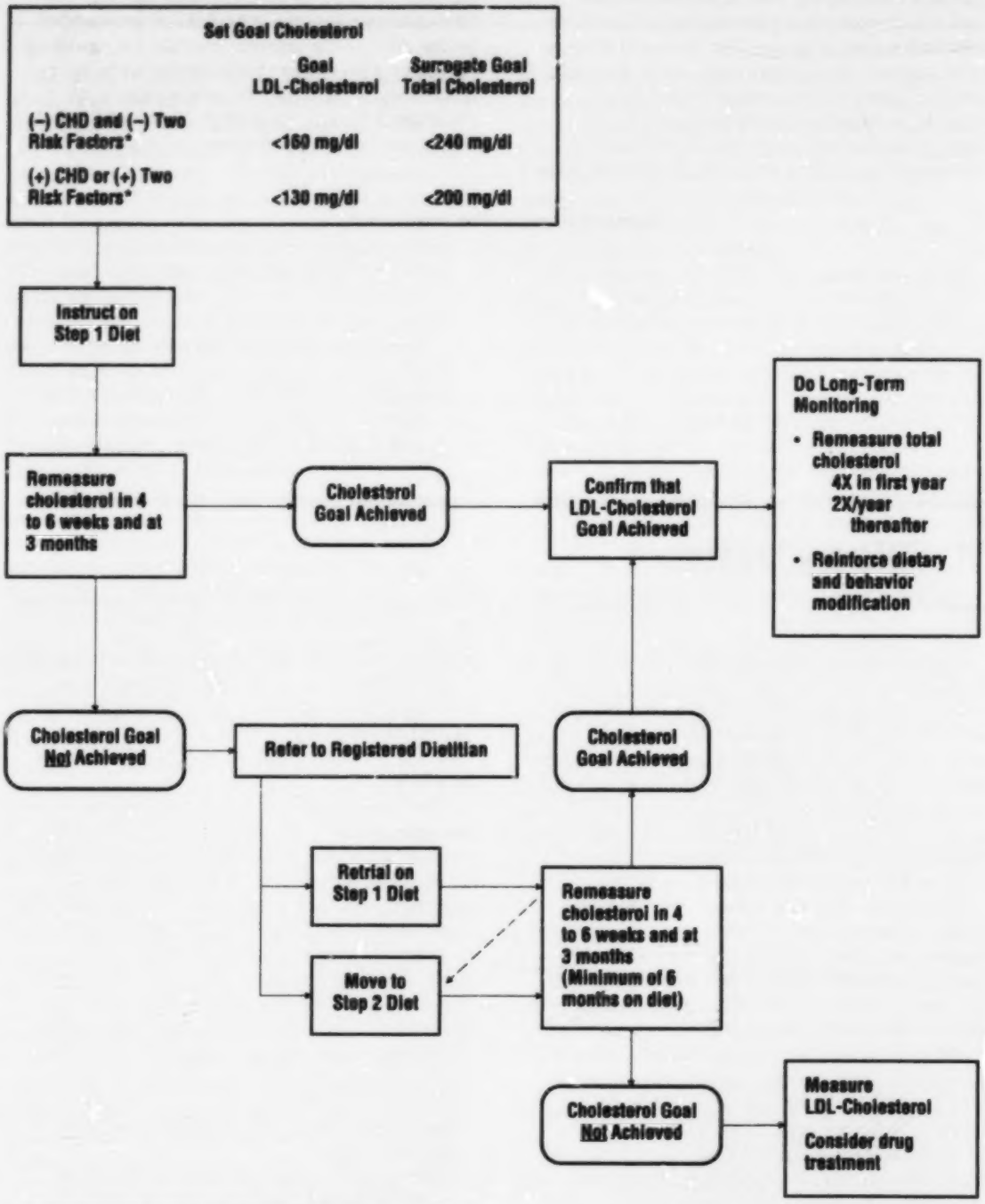
For all patients with elevated blood cholesterol levels, the first line of therapy is diet. The scheme for monitoring and following patients on dietary therapy is summarized in Figure 4. Dietary treatment, including caloric restriction for overweight individuals, is the first step in treating individuals with both high-risk LDL-cholesterol levels (>160 mg/dl) and those with borderline-high-risk LDL-cholesterol levels (130 to 159 mg/dl) who also have definite CHD or two other risk factors. The minimal goals of therapy are: (1) to lower LDL-cholesterol to *below 160 mg/dl* if the patient has neither definite CHD nor two other CHD risk factors; or (2) to lower LDL-cholesterol to *below 130 mg/dl* if definite CHD or two other CHD risk factors are present. *Ideally, dietary means should be used to attain even lower levels of LDL-cholesterol, if possible, to achieve a further reduction in CHD risk.*

Although the goal of therapy is to lower the LDL-cholesterol concentration, measurement of serum total cholesterol can be used to monitor the response to diet. The principle is that LDL-cholesterol should be used for the definitive classification of patients and for decision making, but total cholesterol can be substituted for monitoring. A serum total cholesterol of 240 mg/dl corresponds to an LDL-cholesterol of 160 mg/dl, while a total cholesterol of 200 mg/dl corresponds to an LDL-cholesterol of 130 mg/dl.

The first step in the diet modifications recommended by the ATP (Table 1) are very similar to the diet modifications recommended by the American Heart Association and other organizations for the public at large as part of a population-based approach for lowering cholesterol. However, when applied to patients, these diet recommendations are to be provided in a medical treatment setting in an intensive manner. Accordingly, this dietary intervention is referred to as "dietary treatment." The diets are consistent with good nutrition and aim to achieve healthy eating patterns. The goal is not a temporary "diet," but a permanent change in eating behavior.

Diet modification is planned in two steps, i.e., the Step-One and Step-Two Diets (Table 1). These diets are designed to reduce progressively intakes of saturated fatty acids and cholesterol and eliminate excess calories. The

Figure 4: Dietary Treatment


Set Goal Cholesterol
Goal LDL-Cholesterol
Surrogate Goal Total Cholesterol
(–) CHD and (–) Two Risk Factors*
<160 mg/dl
<240 mg/dl
(+) CHD or (+) Two Risk Factors*
<130 mg/dl
<200 mg/dl
Instruct on Step 1 Diet
Remeasure cholesterol in 4 to 6 weeks and at 3 months
Cholesterol Goal Achieved
Confirm that LDL-Cholesterol Goal Achieved
Do Long-Term Monitoring
• Remeasure total cholesterol 4X in first year 2X/year thereafter
• Reinforce dietary and behavior modification
Cholesterol Goal Not Achieved
Refer to Registered Dietitian
Cholesterol Goal Achieved
Retrial on Step 1 Diet
Move to Step 2 Diet
Remeasure cholesterol in 4 to 6 weeks and at 3 months (Minimum of 6 months on diet)
Cholesterol Goal Not Achieved
Measure LDL-Cholesterol
Consider drug treatment

* One of which can be male sex

Table 1: Dietary Therapy of High Blood Cholesterol

NUTRIENT	RECOMMENDED INTAKE	
	Step-One Diet	Step-Two Diet
Total fat	Less than 30% of total calories	
Saturated fatty acids	Less than 10% of total calories	Less than 7% of total calories
Polyunsaturated fatty acids	Up to 10% of total calories	
Monounsaturated fatty acids	10 to 15% of total calories	
Carbohydrates	50 to 60% of total calories	
Protein	10 to 20% of total calories	
Cholesterol	Less than 300 mg/day	Less than 200 mg/day
Total calories	To achieve and maintain desirable weight	

Step-One Diet should be prescribed by the physician and implemented by the physician and his or her immediate staff. This diet calls for an intake of total fat less than 30 percent of calories, saturated fatty acids less than 10 percent of calories, and cholesterol less than 300 mg/day.

Table 2 illustrates the recommended dietary modifications in each of the food groups in accordance with the Step-One Diet. A copy of this chart can be given to patients along with other educational materials. The patient's serum cholesterol level should be measured at 4 to 6 weeks and at 3 months after starting the Step-One Diet.

If the minimal goals of therapy are not achieved on this diet after 3 months, the patient usually should progress to the Step-Two Diet. Adoption of the Step-Two Diet would be facilitated by referral to a registered dietitian. This diet calls for a further reduction in saturated fatty acid intake to less than 7 percent of calories and cholesterol intake to less than 200 mg/day.

For many patients, the goals of cholesterol lowering can be achieved by dietary therapy alone. For most patients, dietary therapy should be continued for at least 6 months before adding drug therapy. It is important that dietary therapy be given an adequate trial.

The degree of reduction of LDL-cholesterol levels that can be achieved by dietary therapy depends on the existing dietary habits of the patient and on the inherent responsiveness of the patient. In general, patients with high cholesterol levels show a greater absolute reduction in total and LDL-cholesterol concentrations than do individuals with relatively low cholesterol levels. Metabolic ward studies suggest that switching from the typical American diet to the Step-One Diet should reduce cholesterol levels on average by 30 to 40 mg/dl. Advancing to the Step-Two Diet can be expected to cause a further decline of approximately 15 mg/dl in cholesterol levels. Some individuals may demonstrate even greater reductions on the two diets, and others will have lesser responses. Most of the decrease in total blood cholesterol occurs in the LDL fraction.

The major dietary factor that influences blood cholesterol is saturated fat. Dietary cholesterol is important, but the individual response to it is more variable and less consistent than the response to saturated fat. Control of caloric intake is important to maintain or achieve desirable body weight.

Saturated Fatty Acids

Saturated fatty acids have the greatest impact on blood cholesterol when compared to other dietary factors. In the diet, saturated fats raise total blood cholesterol levels and, in particular, LDL-cholesterol. The mechanism by which saturated fatty acids increase LDL has not been determined precisely. However, it appears that saturated fatty acids increase LDL levels by suppressing LDL receptor activity.

Table 2: Recommended Diet Modifications to Lower Blood Cholesterol: The Step-One Diet

	CHOOSE	DECREASE
Fish, Chicken, Turkey, and Lean Meats	Fish, poultry without skin, lean cuts of beef, lamb, pork or veal, shellfish	Fatty cuts of beef, lamb, pork, spare ribs, organ meats, regular cold cuts, sausage, hot dogs, bacon, sardines, roe
Skim and Low-fat Milk, Cheese, Yogurt, and Dairy Substitutes	Skim or 1% fat milk (liquid, powdered, evaporated) Buttermilk	Whole milk (4% fat): regular, evaporated, condensed; cream, half and half, 2% milk, imitation milk products, most nondairy creamers, whipped toppings
	Nonfat (0% fat) or low-fat yogurt	Whole-milk yogurt
	Low-fat cottage cheese (1% or 2% fat)	Whole-milk cottage cheese (4% fat)
	Low-fat cheeses, farmer or pot cheeses (all of these should be labeled no more than 2-6 g fat/ounce)	All natural cheeses (e.g., blue, roquefort, camembert, cheddar, swiss)
		Low-fat or "Light" cream cheese, Low-fat or "Light" sour cream
		Cream cheeses, sour cream
	Sherbet Sorbet	Ice cream
Eggs	Egg whites (2 whites=1 whole egg in recipes), cholesterol-free egg substitutes	Egg yolks
Fruits and Vegetables	Fresh, frozen, canned, or dried fruits and vegetables	Vegetables prepared in butter, cream or other sauces
Breads and Cereals	Homemade baked goods using unsaturated oils sparingly, angel food cake, low-fat crackers, low-fat cookies	Commercial baked goods: pies, cakes, doughnuts, croissants, pastries, muffins, biscuits, high-fat crackers, high-fat cookies
	Rice, pasta	Egg noodles
	Whole-grain breads and cereals (oatmeal, whole wheat, rye, bran, multigrain, etc.)	Breads in which eggs are a major ingredient
Fats and Oils	Baking cocoa	Chocolate
	Unsaturated vegetable oils: corn, olive, rapeseed (canola oil), safflower, sesame, soybean, sunflower	Butter, coconut oil, palm oil, palm kernel oil, lard, bacon fat
	Margarine or shortening made from one of the unsaturated oils listed above	
	Diet margarine	
	Mayonnaise, salad dressings made with unsaturated oils listed above	Dressings made with egg yolk
	Low-fat dressings	
	Seeds and nuts	Coconut

Levels of VLDL and HDL seem to be unaffected by saturated fats. The major sources of saturated fatty acids are animal products, including fatty meats and dairy products such as whole milk, cream, ice cream, butter, and cheese. Although most vegetable oils consist of primarily unsaturated fatty acids, coconut, palm kernel and palm oil are high in saturated fatty acids. Commercially prepared foods such as baked products, convenience foods, and snack foods often contain these so-called tropical vegetable oils or saturated fatty acids provided by butter or lard.

Polyunsaturated Fatty Acids

Polyunsaturated fats include omega-6 fatty acids, such as linoleic acid, and omega-3 fatty acids, such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). In contrast to saturated fatty acids, polyunsaturated fatty acids do not raise serum cholesterol levels. Because there are no data on free-living populations habitually consuming more than 10 percent of their calories from polyunsaturated fats, it has been recommended that the daily intake of polyunsaturated fats should be raised but not exceed 10 percent of total daily calories. In addition, like all fats and oils, polyunsaturated fats are high in total calories, providing more than twice the number of calories as an equal amount of protein and carbohydrates. Consequently they can promote weight gain if consumed in excess of caloric needs.

Omega-6 (Vegetable Oils) The omega-6 polyunsaturated fatty acids such as linoleic acid, found predominantly in safflower, sunflower, soybean, and corn oils, when substituted for saturated fatty acids result in a cholesterol-lowering effect. Although very high intakes of linoleic acid were once advocated for cholesterol lowering, lack of information about the long-term ingestion of large amounts of linoleic acid has led most investigators to recommend a ceiling of 10 percent of total calories.

Omega-3 (Fish Oils) Omega-3 polyunsaturated fatty acids, found primarily in oils of fatty fish, such as salmon and mackerel, inhibit the synthesis of VLDL-triglycerides. Lowering triglycerides appears to be the major effect omega-3 fatty acids have on blood lipids. They usually do not produce much lowering of LDL-cholesterol levels. Since their overall action on other body systems is not well understood, taking omega-3 fatty acid supplements is not recommended. Consumption of omega-3 fatty acids in the form of fish oil supplements should be differentiated from the consumption of fish. Epidemiological studies suggest that persons who frequently eat fish, regardless of its omega-3 content, are at reduced CHD risk. Whether this is true or not, fish is low in saturated fat and thus is a good choice in dietary patterns designed to lower blood cholesterol levels.

Monounsaturated Fatty Acids

The primary monounsaturated fatty acid is oleic acid. It is found in olive oil as well as other oils such as canola oil (rapeseed oil). Other foods also contain significant amounts of monounsaturated fatty acids. Recent evidence indicates that oleic acid may cause as much of a decrease in LDL-cholesterol levels as linoleic acid when substituted for saturated fatty acids. Thus, substituting monounsaturated fats, like substituting polyunsaturated fats, for saturated fats reduces blood cholesterol levels. The recommended intake for monounsaturated fat is 10 to 15 percent of total daily calories.

Dietary Cholesterol

Dietary cholesterol is found in varying amounts in all foods of animal origin but not in foods of plant origin. Particularly rich sources are egg yolk and organ meats (liver, sweetbreads, and brain). Some shellfish (e.g., shrimp) also are moderately high in cholesterol, but not to the extent of egg yolk or organ meats. Overall, excess dietary cholesterol appears to raise LDL-cholesterol levels, although its effect is less predictable than that of saturated fats. The degree of rise varies from person to person. Furthermore, concern about dietary cholesterol extends beyond its effects in raising the LDL-cholesterol level. Newly absorbed cholesterol enters the circulation with chylomicrons, which are degraded to cholesterol-rich chylomicron remnants; the latter may be atherogenic. Dietary cholesterol is not required for normal body function.

Body Weight and Calories

Obesity is not only associated with elevated serum LDL-cholesterol levels but is an independent risk factor for CHD. *An important recommendation therefore is to reduce caloric intake to achieve weight reduction in overweight patients.* Weight reduction will lower the LDL-cholesterol level in many people, as well as reduce plasma triglycerides and raise HDL-cholesterol levels. Some patients with high-risk LDL-cholesterol levels are extremely sensitive to caloric intake, and weight reduction and establishment of desirable body weight will completely correct their elevated LDL-cholesterol concentrations. *The importance of caloric restriction in overweight, high-risk individuals cannot be overemphasized.*

Weight reduction can be facilitated by exercise. Regular exercise will burn up calories as well as help curb the appetite. It also will lower serum triglycerides, raise HDL-cholesterol levels, and, in some individuals, may lower the LDL-cholesterol level.

Carbohydrates

Dietary carbohydrates include simple sugars, complex digestible carbohydrates (starches), and complex indigestible carbohydrates (fiber). In most people, when digestible carbohydrates are substituted for saturated fatty acids, the LDL-cholesterol level will fall to about the same extent as when oleic acid and linoleic acid are substituted for saturated fat. Complex carbohydrates should comprise more than half of digestible carbohydrate intake. Very high-carbohydrate diets (e.g., 80 to 90 percent of calories) can raise plasma triglycerides, but triglycerides are not usually elevated when fat intakes are in the vicinity of 30 percent of calories.

Indigestible carbohydrates that are water soluble also have an effect on plasma cholesterol. This category includes pectins, certain gums, and psyllium. One of the gums is beta-glucan, which is present in oat products and beans. High intakes (e.g., 15 to 25 grams per day) of soluble fiber have been reported to lower the plasma cholesterol level by 5 to 15 percent. These high intakes can produce gastrointestinal side effects, but prolonged usage frequently is associated with improved tolerance.

Dietary Adherence

Many patients will achieve the target goals for lowering of LDL-cholesterol with dietary therapy. Adherence to the diet is facilitated by monitoring the patient's total cholesterol level which should be carried out on a long-term basis. Because the fat-modified diet is to be maintained indefinitely, the patient should receive sufficient information to make dietary change, as well as encouragement and reinforcement to adhere to the recommended eating pattern. The patient who has achieved his or her LDL-cholesterol goal should be counseled quarterly for the first year of long-term monitoring and twice yearly thereafter. Total serum cholesterol should be measured prior to each visit, and the results should be used at the subsequent counseling session.

Many patients with initial high cholesterol levels are "diet sensitive," which explains their originally high level. Thus attention must be given to continued dietary adherence to avoid a "relapse" to high cholesterol concentrations. If the patient redevelops an elevated cholesterol level, the action plan outlined above for dietary therapy of elevated LDL-cholesterol may have to be reinstituted.

If diet is to succeed as the cornerstone of high blood cholesterol management, patients need practical guidance to implement the recommended dietary changes.

The following tips have been useful to clinicians:

- The cholesterol-lowering diet should be presented with a positive perspective. The physician should discuss (a) the efficacy, safety, and nutritional adequacy of the diet; (b) the potential for choosing appetizing foods and satisfying meals; and (c) the relative ease of gradual adaptation to the new dietary plan.
- The entire family, including the food preparer, should receive the information provided to the patient regarding dietary treatment.

- Realistic goals need to be set and closely monitored.
- Dietary modifications are usually accomplished if initiated gradually over a period of time. People need sufficient time to apply information learned to food purchases, preparation and eating away from home. They find it easier to make small changes in a short period of time.
- The patient may need to consult a registered dietitian for detailed diet counseling.
- The patient should be given information on grocery shopping, food preparation, entertaining, and eating away from home.
- The National Heart, Lung, and Blood Institute has free patient education materials that explain the concepts of blood cholesterol and its relation to coronary heart disease, and offer practical advice for following dietary guidelines to lower elevated blood cholesterol levels. The two available patient education pamphlets are entitled, "So You Have High Blood Cholesterol" and "Eating to Lower Your High Blood Cholesterol." For more information, you and your patients can contact: National Cholesterol Education Program, National Institutes of Health, National Heart, Lung, and Blood Institute, C-200, Bethesda, Maryland 20892.

VII. Drug Treatment

Maximal efforts should be made in all patients to lower blood cholesterol levels and CHD risk by nonpharmacologic approaches such as diet, weight control, exercise, and other lifestyle modifications. If an individual's LDL-cholesterol level remains significantly elevated after an adequate trial of maximal dietary intervention–in most cases after at least 6 months of intensive dietary therapy–supplementary drug therapy should be considered. Drugs, however, are not a substitute for diet. When patients combine dietary with drug treatment, the *beneficial effect is additive*, and the dose of the drug can be minimized. Hence, maximal efforts at dietary therapy should be made before initiating drug therapy and should be continued even if drug therapy is needed.

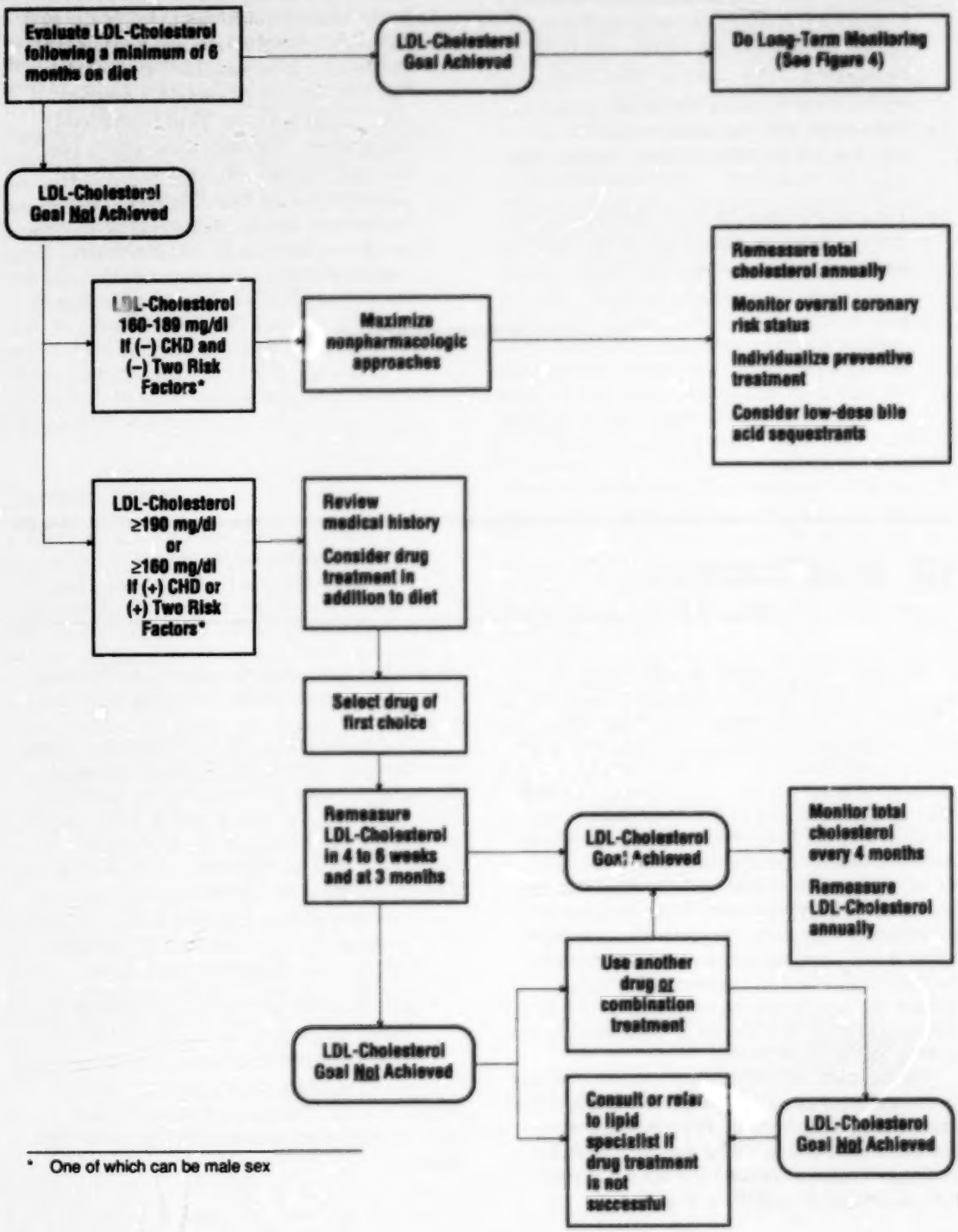
The decision to initiate drug treatment usually commits the patient to long-term therapy, for many years, even for life. Because the potential number of patients who are candidates for prolonged administration of drugs is substantial, all decisions to initiate drug therapy should be made only after careful deliberation. Dietary therapy is clearly the safest treatment available.

LDL-cholesterol is the best parameter to use in making the decision to begin drug therapy for monitoring the response to drug therapy (at least in the first few months). The LDL-cholesterol levels at which drug therapy should be considered after an adequate trial of dietary therapy alone are as follows:

- ≥190 mg/dl (very high-risk LDL-cholesterol): In patients without definite CHD or two other CHD risk factors.
- ≥160 mg/dl (high-risk LDL-cholesterol): In patients with definite CHD or two other CHD risk factors.

Figure 5 outlines the drug treatment plan based on LDL-cholesterol levels and summarizes suggested action steps for the various levels.

Figure 5: Drug Treatment


Evaluate LDL-Cholesterol following a minimum of 6 months on diet
LDL-Cholesterol Goal Achieved
Do Long-Term Monitoring (See Figure 4)
LDL-Cholesterol Goal Not Achieved
LDL-Cholesterol 160-189 mg/dl If (–) CHD and (–) Two Risk Factors*
Maximize nonpharmacologic approaches
Remeasure total cholesterol annually
Monitor overall coronary risk status
Individualize preventive treatment
Consider low-dose bile acid sequestrants
LDL-Cholesterol ≥190 mg/dl or ≥160 mg/dl If (+) CHD or (+) Two Risk Factors*
Review medical history
Consider drug treatment in addition to diet
Select drug of first choice
Remeasure LDL-Cholesterol in 4 to 6 weeks and at 3 months
LDL-Cholesterol Goal Achieved
Monitor total cholesterol every 4 months
Remeasure LDL-Cholesterol annually
Use another drug or combination treatment
LDL-Cholesterol Goal Not Achieved
Consult or refer to lipid specialist if drug treatment is not successful
LDL-Cholesterol Goal Not Achieved

* One of which can be male sex

Clinical judgment is required when using these guidelines to make decisions about initiating drug therapy. All individuals with LDL-cholesterol levels ≥190 mg/dl are candidates for drug therapy, but the need is less pressing in the older female. Men with LDL-cholesterol values between 160 and 190 mg/dl who have any other major CHD risk factor generally should receive drug therapy. In women, however, a more conservative approach to drug therapy is appropriate, in view of the fact that the absolute risk of CHD is lower in women than in men.

When choosing a specific drug and its dosage, the nature of the lipid disorder and the availability of long-term safety data on the drug must be considered. The cost of the various drugs also warrants some consideration and should be viewed in relation to a drug's effectiveness and safety in cholesterol lowering. Drug treatment should be undertaken cautiously and reevaluated often.

The minimal goals of drug therapy are the same as those of dietary therapy (see page 11), and are as follows:

- LDL-cholesterol <160 mg/dl: In patients without definite CHD or two other CHD risk factors (one of which can be male sex).
- LDL-cholesterol <130 mg/dl: In patients with definite CHD or two other CHD risk factors.

The major drugs for consideration include: bile acid sequestrants (cholestyramine and colestipol), nicotinic acid, the HMG CoA reductase inhibitors, gemfibrozil, and probucol. The bile acid sequestrants and nicotinic acid are considered the drugs of first choice on the basis that they have been found to produce good reductions in cholesterol levels, to reduce CHD risk, and to be generally safe in long-term use.

Bile Acid Sequestrants

The major effect of the bile acid sequestrants is to decrease LDL-cholesterol. These drugs are contraindicated as single drug therapy in patients with marked hypertriglyceridemia (>500 mg/dl) and in patients with a history of severe constipation. The sequestrants are not absorbed from the gastrointestinal tract and lack systemic toxicity. The disadvantages of the sequestrants are related to the method of administration and the frequency of gastrointestinal side effects.

The primary action of the sequestrants is to bind bile acids in the intestinal lumen. This interrupts the enterohepatic circulation of bile, forcing the liver to convert more cholesterol to bile acids. Despite a compensatory increased rate of hepatic cholesterol synthesis, there is a net decrease in hepatic cholesterol that stimulates hepatic LDL receptor production. More LDL receptors lead to increased uptake of LDL-cholesterol, resulting in a decrease in plasma levels of LDL.

Cholestyramine and colestipol are two bile acid sequestrants. Cholestyramine was used in the CPPT, which documented that lowering LDL reduces the risk of CHD. Cholestyramine lowers total and LDL-cholesterol levels and raises HDL-cholesterol levels slightly. Reductions of 20 to 25 percent in total cholesterol and 25 to 30 percent in LDL-cholesterol have been reported. In the CPPT, the cholestyramine patients who took 16 to 24 grams a day reduced their total cholesterol level by 25 percent and reduced CHD risk by 49 percent.

Colestipol (used together with nicotinic acid in the Cholesterol Lowering Atherosclerosis Study) has an LDL-lowering effect equivalent to that of cholestyramine and essentially the same mechanism of action.

Nicotinic Acid

Nicotinic acid, also known as the B vitamin niacin, is indicated for therapy of both LDL and VLDL elevations. In people treated with nicotinic acid, it has been shown to cause a reduction in long-term cardiovascular and total mortality. Pharmacologic doses of nicotinic acid substantially reduce total cholesterol levels, LDL-cholesterol levels and VLDL levels, and increase HDL levels. Decreases of 25 percent in total cholesterol levels may be observed. The doses associated with nicotinic acid's use as a vitamin do not have these lipid lowering effects.

Nicotinic acid has been shown to decrease CHD risk in clinical trials, and its long-term safety has been established, although it does produce some important side effects such as flushing of the skin, hyperuricemia, and abnormalities in liver function. It is the least costly

of currently available agents. Flushing is greatly reduced by slowly increasing nicotinic acid to full dose, avoiding administration on an empty stomach, and by pre-treatment with aspirin or non-steroidal anti-inflammatory drugs. The use of sustained-release preparations also will reduce flushing, but their cost is considerably greater.

Nicotinic acid appears to interfere with adipose tissue lipolysis, decreasing the supply of free fatty acids used for VLDL production by the liver, which results in decreased circulating VLDL levels. Since VLDL is the precursor of most LDL, a reduction in the synthesis of VLDL decreases LDL synthesis. Nicotinic acid may also inhibit cholesterol synthesis. Nicotinamide is not to be confused with nicotinic acid. Nicotinamide is not effective in lowering LDL-cholesterol and cannot substitute for nicotinic acid.

HMG CoA Reductase Inhibitors

The discovery of specific competitive inhibitors of the rate-limiting enzyme in cholesterol biosynthesis (HMG CoA reductase) has opened up a new avenue of therapy for patients with primary hypercholesterolemia. A number of drugs in this category are being evaluated including lovastatin, simvastatin, and pravastatin. Of these, lovastatin has been most extensively studied in humans and was approved by the FDA for prescription use in September 1987. Long-term safety information is limited or not available, and thus caution in its use is recommended. This is especially true for individuals who are not at high risk.

Although the effects of HMG CoA reductase inhibitors on CHD incidence have not yet been established, mean reductions in LDL-cholesterol of 25 to 45 percent have been noted in both familial and nonfamilial forms of hypercholesterolemia. HMG CoA reductase inhibitors increase LDL receptor activity in the liver and increase the rate of receptor-mediated removal of LDL from plasma. The production of LDL is also decreased.

If long-term safety can be satisfactorily established, these inhibitors of cholesterol biosynthesis will represent a major advance in the therapy of hypercholesterolemia. These agents are extremely effective in reducing LDL-cholesterol concentrations and, from the patient's point of view, are easy to take.

Gemfibrozil

Gemfibrozil, a fibric acid derivative, is approved by the FDA primarily for triglyceride lowering to reduce the risk of pancreatitis, and not for routine use in lowering cholesterol to reduce the risk of CHD. It has sometimes been used as single drug therapy in patients who do not tolerate the bile acid sequestrants or nicotinic acid and has occasionally been used in combination with first choice drugs. The Helsinki Heart Study, published in November 1987, was a 5-year trial that tested the clinical efficacy and safety of gemfibrozil (600 mg twice daily) versus placebo in 4,081 asymptomatic middle-aged men with elevated blood cholesterol levels. Gemfibrozil moderately reduced serum levels of total and LDL-cholesterol and of triglycerides, and moderately increased HDL levels. In this group, the incidence of CHD was reduced by 34 percent ($p<0.02$). This trial thus provided evidence on the clinical efficacy and safety of gemfibrozil in reducing coronary risk in patients with high cholesterol levels. In view of these results, it would be reasonable for physicians to consider the use of gemfibrozil more readily when selecting drugs for patients with high cholesterol levels who meet the criteria for drug treatment. Gemfibrozil may be particularly useful, as an alternative to nicotinic acid, in patients with high-risk LDL-cholesterol levels who also have borderline hypertriglyceridemia (triglyceride levels 250 to 500 mg/dl) and low HDL-cholesterol levels. More extensive review and evaluation of the results of the Helsinki Heart Study may clarify further the place of gemfibrozil in the treatment of patients with high blood cholesterol.

Probucol

Probucol therapy usually reduces LDL-cholesterol by about 8 to 15 percent, but there is also an associated reduction in HDL-cholesterol of up to 25 percent. There are no extensive, long-term clinical studies currently available for assessing probucol's safety or effect on CHD risk. Preliminary information indicates that probucol may inhibit the oxidation and tissue deposition of LDL. Probucol increases the rate of LDL catabolism, part of which may involve nonreceptor-mediated pathways. The role of probucol in the treatment of patients with high LDL-cholesterol is uncertain

because of concerns about the reduction in HDL-cholesterol, but xanthoma regression has also been reported as the HDL-cholesterol level decreases. Probucol is sometimes used as single drug therapy in patients who do not tolerate other drugs and is occasionally used in combination with first choice drugs.

Clofibrate

Clofibrate, like gemfibrozil, is a fibric acid derivative. It is approved by the FDA primarily for triglyceride lowering to reduce the risk of pancreatitis and not for routine use in lowering cholesterol to reduce the risk of CHD. Clofibrate is used less frequently than gemfibrozil, however, because of reports of long-term toxicity in clinical trials, particularly the WHO Clofibrate Study.

Adherence to Drug Therapy

With good adherence to drug treatment, maximum lowering of LDL-cholesterol is obtained within 4 weeks of initiating drug therapy. Thus, the first repeat LDL-cholesterol determination should be made 4 to 6 weeks after initiating drug therapy. A second measurement should be done at 3 months; a minimum of two lipoprotein determinations is essential for evaluating drug efficacy. The mean of these two determinations and a careful assessment of drug adherence should be used to initially judge the effectiveness of drug treatment. After the response to drug therapy has been established and if the response is adequate, then the patient should be seen for a followup visit approximately every 4 months, in order to monitor for side effects and assess the patient's status and response to therapy. A "lipoprotein profile" (LDL-cholesterol measurement) at yearly intervals will usually be adequate; measurement of serum total cholesterol will usually suffice for the interim visits.

If the patient has had at least a 15-percent decrease in LDL-cholesterol and is tolerating the drug but has not achieved the minimum target goal for LDL-cholesterol, consideration should be given to adding another drug. If the patient has not had a 15-percent decrease in LDL-cholesterol or is not tolerating the drug, the physician should either switch to another drug or proceed to combination therapy, if necessary. Consultation with a lipid specialist may be useful in the management of patients with persistently high LDL-cholesterol levels despite dietary and drug therapy.

Since drug therapy to lower blood cholesterol involves a lifelong commitment, adherence to treatment regimens is essential. The key to adherence lies in patient education. All patients should know the magnitude of their health problems and the significance of their management regimens.

To promote adherence, consider the following points:

- In addition to selecting a drug based on safety and efficacy, consult with the patient to find a drug that he or she can tolerate.
- Offer substantial patient education to promote adherence to the bile acid sequestrants and nicotinic acid, especially during the early stages of treatment.
- Introduce self-monitoring and review records at follow-up appointments.
- Begin with a small dose and gradually adjust it upward to allow the patient's system to adapt to the new drug.
- Discuss the drug's side effects and methods to minimize those effects.
- Discuss methods of drug preparation in the case of bile acid sequestrants in an attempt to find the preparation best suited for the patient's comfort and tolerance.
- Provide practical advice so that the treatment regimen can be incorporated into the patient's current lifestyle.
- Be aware that health professionals already involved in patient education are a logical source of help for the patient who is having problems with side effects. A sensitive, caring individual who routinely sees the patient can be an important component of effective adherence counseling.
- Consider adapting standard patient education materials for individual regimens.
- Consider undertaking inexpensive followup by telephone or mail between office visits to help maintain adherence.

VIII. The Importance of a Multidisciplinary Team Approach

Successful cholesterol-lowering interventions depend upon cooperation among physicians, registered dietitians, nurses, pharmacists, and other health professionals, who must work together as a team. After the physician has diagnosed the patient and established the treatment regimen, the other members of the health care team play a critical role in treatment and followup. The treatment interventions are also the responsibility of the patients, for whom the challenge is to make the dietary and other lifestyle changes that are needed for successful reduction of CHD risk.

IX. Ongoing Efforts of the National Cholesterol Education Program

The NCEP will continue to focus on providing health care professionals and the public with updated information and guidance so they can make more effective decisions regarding the detection and treatment of high blood cholesterol. The information in the ATP report, for example, is being disseminated by way of a kit of materials developed for physicians, and by patient education materials, continuing medical education activities, and presentations at professional meetings.

The Laboratory Standardization Panel is addressing issues that relate to laboratory measurement of blood cholesterol. Initial recommendations call for all U.S. laboratories to adopt the cholesterol cutpoints recommended in the Adult Treatment Panel report and cited in this monograph. The panel also recommends that bias of current cholesterol measurement methods should not exceed ± 5 percent from true value and should be no greater than ± 3 percent from true value within 3 years. All laboratories should use certified reference materials available from the National Bureau of Standards, the Centers for Disease Control, or the College of American Pathologists.

In addition, a Population-Based Panel established in February 1988 is currently examining the most effective and appropriate approaches for lowering blood cholesterol in the general population. A Treatment Panel on Children and Adolescents will be convened to address the specific and somewhat more complex issues of diet and drug intervention to lower high blood cholesterol levels in children. The population-based (public health) approach complements the patient-based approach described in this monograph. Together, they represent a coordinated strategy aimed at reducing cholesterol levels and the risk for coronary heart disease.

The NCEP also has initiated a public education campaign with a "Know Your Cholesterol" theme. The major goal of this campaign is to increase public awareness of the dangers of high

blood cholesterol, the importance of having blood cholesterol levels checked, and the significance of those levels. These messages are being conveyed through radio and television public service announcements, print ads, publications, and fact sheets. All the information disseminated by the NCEP is based on the latest scientific evidence. While the current data are extensive, many questions about the etiological and pathophysiological aspects of high blood cholesterol remain. As knowledge is obtained in this dynamic field, it will continue to be conveyed to the scientific, medical, public health, and lay communities in a timely and responsible manner.

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CME Quiz

Cholesterol: Current Concepts for Clinicians

This quiz offers you the opportunity to assess your knowledge and retention of the information presented in this monograph and to earn continuing medical education credit. As an organization accredited for continuing medical education, Hahnemann University certifies that this CME instruction has been planned, produced, and distributed and that it is being evaluated in compliance with the ACCME Essentials for CME.

Members of the medical faculty at Hahnemann University have reviewed the manuscript and certify that it meets the criteria for 2 credit hours in Category 1 of the Physician's Recognition Award of the American Medical Association, provided it is used and completed as designed.

To earn credit, carefully read the preceding monograph and answer the questions below. Mark your answers by placing an X in the proper squares, under A, B, C, D, or E, and mail the test to Hahnemann University for certification. (See end of test for details.) To earn credit, answers must meet minimum score criteria of 70 percent correct and must be received by the Office for Continuing Education by October 30, 1989. The quiz may be submitted only once for credit. However, extended answers will be sent to ALL persons submitting the test for credit regardless of whether or not they pass. The extended answers will be available to others on request after October 30, 1989.

	A	B	C	D	E
1. The primary cause of CHD is a type of arteriosclerosis that affects a. large arteries b. small arteries c. arteries of any size	❑	❑	❑	❑	❑
2. It has been shown that lowering blood cholesterol levels can a. slow the atherogenic process b. lead to regression of existing lesions c. both a and b above d. none of the above	❑	❑	❑	❑	❑
3. Data from the Coronary Primary Prevention Trial a. suggested that cholesterol levels somewhat below 200 mg/dl may carry an increased risk of CHD b. provided conclusive evidence that decreasing high cholesterol levels decreases the rate of heart attacks c. demonstrated that by reducing LDL-cholesterol the incidence of CHD mortality could be reduced d. b and c above e. all of the above	❑	❑	❑	❑	❑

	A	B	C	D	E
4. The aggressively treated group of subjects in the 1987 Cholesterol-Lowering Atherosclerosis Study	❑	❑	❑	❑	❑
a. demonstrated a substantial reduction in LDL- and HDL-cholesterol levels					
b. received diet, colestipol and nicotinic acid therapy					
c. less than 40 percent had progression of atherosclerotic lesions					
d. b and c above					
e. all of the above					
5. Most of the circulating cholesterol in the blood normally is carried in	❑	❑	❑	❑	❑
a. LDL					
b. VLDL					
c. IDL					
d. HDL					
6. In the exogenous pathway of the lipoprotein system,	❑	❑	❑	❑	❑
1. products of lipid digestion are assembled in the intestinal wall into chylomicrons					
2. chylomicrons are transported into the peripheral circulation through the thoracic-lymphatic system					
3. in muscle capillaries and in adipose tissue the enzyme lipoprotein lipase hydrolyzes triglycerides					
4. some IDL is removed from the circulation by LDL receptors in the liver					
a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4					
7. When there is an oversupply of cholesterol available to the cell surface, the manufacture of LDL receptors is	❑	❑	❑	❑	❑
a. not affected					
b. increased					
c. inhibited					
8. In familial hypercholesterolemia, there is an increased number of LDL receptors on cell surfaces	❑	❑	❑	❑	❑
a. True b. False					

	A	B	C	D	E
9. The NCEP ATP listing of risk factors for CHD includes	❑	❑	❑	❑	❑

1. male sex
2. HDL concentration less than 35 mg/dl
3. presence of diabetes mellitus
4. severe obesity

a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4

10. The serum cholesterol level at which CHD risk is almost double that at 200 mg/dl is	❑	❑	❑	❑	❑

a. 320 mg/dl
b. 280 mg/dl
c. 240 mg/dl
d. 220 mg/dl

11. Patients with LDL-cholesterol levels of 130 to 159 mg/dl and no CHD or risk factors should	❑	❑	❑	❑	❑

a. be advised to follow a fat-modified diet
b. re-evaluated annually
c. both a and b above
d. none of the above

12. Patients with borderline high-risk LDL-cholesterol levels and CHD or two CHD risk factors should aim for reducing the LDL-cholesterol levels to 140 mg/dl	❑	❑	❑	❑	❑

a. True b. False

13. The NCEP's ATP recommends that serum total cholesterol should be measured	❑	❑	❑	❑	❑

a. in all adults age 35 and over
b. every two years
c. both a and b above
d. none of the above

14. An accurate determination of serum total cholesterol levels requires	❑	❑	❑	❑	❑

1. testing in the fasting state
2. that patients be in their usual state of health
3. blood to be collected as serum
4. confirmation of cholesterol levels of >200 mg/dl by repeat measurements

a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4

	A	B	C	D	E
15. If a patient's LDL-cholesterol level is determined to be 185 mg/dl on the first measurement and 205 mg/dl eight weeks later,	❑	❑	❑	❑	❑

a. a third measurement should be obtained
b. the 205 mg/dl should be used for clinical decisions
c. an average of the two measurements should be used for clinical decisions
d. none of the above

16. In the Step-One diet for reduction of blood cholesterol levels it is recommended that	❑	❑	❑	❑	❑

1. saturated fatty acids make up less than 10 percent of total calories
2. monounsaturated fats make up 10 to 15 percent of total calories
3. carbohydrates make up 50 to 60 percent of total calories
4. cholesterol be limited to less than 300 mg/day

a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4

17. In both the Step-One and Step-Two diets, total fat should make up less than 30 percent of total calories.	❑	❑	❑	❑	❑

a. True b. False

18. The major dietary factor that influences blood cholesterol levels is	❑	❑	❑	❑	❑

a. dietary cholesterol
b. saturated fat
c. monounsaturated fat
d. none of the above

19. Which of the following vegetable oils is/are highly saturated?	❑	❑	❑	❑	❑

1. sesame oil
2. palm kernel oil
3. olive oil
4. coconut oil

a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4

	A	B	C	D	E
20. Omega-3 polyunsaturated fatty acids	❑	❑	❑	❑	❑

a. inhibit the synthesis of VLDL triglycerides
b. increase HDL levels
c. substantially reduce LDL-cholesterol levels
d. a and b above
e. all of the above

21. Substituting monounsaturated fats for saturated fats has been found to reduce blood cholesterol levels. ❑ ❑ ❑ ❑ ❑

a. True b. False

22. Exercise has been found to ❑ ❑ ❑ ❑ ❑

a. reduce serum triglyceride levels
b. increase HDL-cholesterol levels
c. reduce LDL-cholesterol levels
d. a and b above
e. all of the above

23. Diets high in soluble fiber have not been found to have an effect upon plasma cholesterol levels. ❑ ❑ ❑ ❑ ❑

a. True b. False

24. Which of the following statements is/are true regarding the bile acid sequestrants? ❑ ❑ ❑ ❑ ❑

1. They primarily lower LDL-cholesterol
2. They are well-absorbed from the GI tract
3. Their mechanism of action is to bind bile acids in the intestinal lumen
4. They may be used as monotherapy in patients with marked hypertriglyceridemia

a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4

25. Pharmacologic doses of nicotinic acids substantially reduce ❑ ❑ ❑ ❑ ❑

a. total cholesterol levels
b. LDL-cholesterol levels
c. VLDL levels
d. a and b above
e. all of the above

	A	B	C	D	E
26. Nicotinamide can be substituted for nicotinic acid for reduction of LDL levels.	❑	❑	❑	❑	❑
a. True b. False					
27. HMG CoA reductase inhibitors	❑	❑	❑	❑	❑
1. increase LDL receptor activity in the liver					
2. increase the rate of receptor-mediated removal of LDL from plasma					
3. decrease the production of LDL					
4. increase the production of HDL					
a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4					
28. The fibric acid derivative, gemfibrozil	❑	❑	❑	❑	❑
1. reduces total cholesterol levels					
2. increases triglycerides					
3. increases HDL-cholesterol levels					
4. reduces LDL-cholesterol levels					
a. 1,2 b. 2,4 c. 3 only d. 1,2,3,4 e. 1,3,4					
29. With good drug adherence, maximum lowering of LDL-cholesterol is obtained within _____ of initiating drug therapy.	❑	❑	❑	❑	❑
a. 6 months					
b. 4 months					
c. 10 weeks					
d. 4 weeks					
30. Adherence to drug therapy for lowering LDL-cholesterol levels may be promoted by	❑	❑	❑	❑	❑
1. beginning with small doses and gradually adjusting dosage upward					
2. discussing the drug's side effects and methods to minimize those effects					
3. providing for followup between visits					
4. adapting standard patient education materials for individual regimens					
a. 1,2,3 b. 1,3 c. 2,4 d. 4 only e. 1,2,3,4					

Complete the information below. Then send this form, the quiz, the evaluation form, and a check in the amount of $12.00 made out to Hahnemann University* to:

Office for Continuing Education, M.S. 623
Hahnemann University
Broad and Vine Streets
Philadelphia, PA 19102

Upon passing, a certificate of completion will be mailed verifying your score and awarding CME Category I credits. Regardless of your score, you will receive your corrected quiz and a set of explanatory, extended answers. For credit, the quiz and payment must reach the Office for Continuing Education no later than October 30, 1989.

PLEASE TYPE IN THE INFORMATION BELOW

Your Speciality _____

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* The payment covers all processing and administrative costs for the awarding of CME credit.

Monograph Evaluation Form

Cholesterol: Current Concepts for Clinicians

Dear Doctor:

Your interest in this monograph is appreciated. As we continue to develop programs for CME purposes, your input is critical to proper planning. Therefore, we would appreciate it if you could take a few minutes to fill in the following questionnaire and return it to the following address:

Office for Continuing Education, M.S. 623
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Broad and Vine Streets
Philadelphia, PA 19102

1. The monograph met its stated objectives.

Strongly agree				Strongly disagree
1	2	3	4	5

2. The monograph was well prepared.

Strongly agree				Strongly disagree
1	2	3	4	5

3. This is a good educational format.

Strongly agree				Strongly disagree
1	2	3	4	5

4. The quiz presented a good overall assessment of the information.

Strongly agree				Strongly disagree
1	2	3	4	5

5. Comments: _____

_____

_____

6. What other types of CME programs would you be interested in participating in?

- ❑ Symposiums
- ❑ Videotape Programs
- ❑ Computer-Assisted Learning
- ❑ Telephone Conference
- ❑ Audiotape Programs
- ❑ Visiting Professors
- ❑ Monographs
- ❑ Tutorials

7. Suggested topics for future programs: _____

_____

_____

Cholesterol Resources for the Physician

As a physician, you may need additional resources on high blood cholesterol to help you in your practice and in counseling your patients. You may also want to provide information and printed materials to your patients who have high blood cholesterol.

The organizations listed here provide information on coronary heart disease, diet, and cholesterol-lowering drugs. These organizations may also provide diet counseling services or referrals to registered dietitians. The American Dietetic Association maintains a roster of registered dietitians and responds to written requests for assistance in locating a registered dietitian in a given area. State dietetic associations, the American Heart Association, public health departments, as well as the nutrition departments of universities often will recommend nutrition counselors. Local groups and chapters of national organizations will be most helpful and should be contacted first.

Information Resources	Contact	What to Request

I. Government

U.S. Department of Health and Human Services

National Institutes of Health, National Cholesterol Education Program National Heart, Lung, and Blood Institute C-200 Bethesda, MD 20892 (301) 951-3260	Information Specialist	**Professional:** *Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults* *Highlights of the Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults* *Public Screening for Measuring Blood Cholesterol—Issues for Special Concern* *Current Status of Blood Cholesterol Measurement in Clinical Laboratories in the United States* *Community Guide to Cholesterol Resources* *Heart to Heart: A Manual on Nutrition Counseling for the Reduction of Cardiovascular Disease Risk Factors* **Patient:** *So You Have High Blood Cholesterol* *Eating to Lower Your High Blood Cholesterol* *The Healthy Heart Handbook for Women* *Healthy Heart I.Q.* *Facts About . . . Blood Cholesterol*

Information Resources	Contact	What to Request
Food and Drug Administration, Office of Consumer Affairs, HFE-88 5800 Fishers Lane Rockville, MD 20857 (301) 443-3170 U.S. Government Listing of your regional Office*	Consumer Affairs Department/Consumer Inquiries Department	**Patient:** *FDA Consumer* (a series on selected topics) Information on food labeling, and on the fat and cholesterol composition of foods
U.S. Department of Agriculture		
Extension Service County/State Government Listing: "Cooperative Extension" or "Extension"	Food and Nutrition Specialist	Publications vary from state to state Low-fat, low-cholesterol cooking information
Human Nutrition Information Service Room 360 Federal Building 6505 Belcrest Road Hyattsville, MD 20782 (301) 436-8474	Information Specialist	**Patient:** *Dietary Guidelines for Americans* *Mini Bulletin: Avoid Too Much Fat, Saturated Fat, and Cholesterol, Home and Garden Bulletin 232-3*
Food and Nutrition Information Center National Agricultural Library Building Room 304 Route 1 Beltsville, MD 20705 (301) 344-3719	Information Specialist/Nutritionist	**Professional and Patient:** Pathfinder—Dietary Fat and Heart Disease
Public Health Departments County/State Government Listings: "Public Health" or "Health"*	Registered Dietitian/Nutritionist	Publications vary from state to state Nutrition counseling

Information Resources	Contact	What to Request

II. Professional

The American Dietetic Association 430 North Michigan Avenue Chicago, IL 60611 (312) 280-5000 Call national headquarters or check business listings. Yellow Pages: "Associations"*	Nutrition Resources Department	**Professional:** *Hyperlipidemia: Lipid Metabolism and Food Patterns* **Patient:** *The Dieter's Guide* *Food 3: Eating the Moderate Fat and Cholesterol Way* Nutritionists/Dietitians in private practice.
American Heart Association National Center 7320 Greenville Avenue Dallas, TX 75231 (214) 750-5300 Local business listing: "American Heart" or "Heart Association"*	Nutritionist/Health Educator/Program Specialist	**Professional:** *Dietary Treatment of Hypercholesterolemia: A Manual for Counselors* *Counseling the Patient with Hyperlipidemia* *Counseling Adolescents for Dietary Changes* *Coronary Risk Handbook: Estimating Risk* **Patient:** *Dietary Treatment of Hypercholesterolemia: A Manual for Patients* *Nutrition Counseling for Cardiovascular Health: A Consumer Guide* *Cholesterol and Your Heart* *The American Heart Association Diet* *Recipes for Fat Controlled Low Cholesterol Meals* *Dining Out*

Information Resources	Contact	What to Request
Society for Nutrition Education 1700 Broadway Suite 300 Oakland, CA 94612 (415) 444-7133	Publications Department	**Patient:** SNE has developed films and publications on health and nutrition, notably *The Family Health Cookbook*, which lists the fat and cholesterol content of recipes.
American Pharmaceutical Association 2215 Constitution Avenue, N.W. Washington, DC 20037 (202) 628-4410	Professional Affairs Department	APhA can connect callers with local pharmacists active in health promotion programs. Slide/tape programs are available for presentation by health professionals.

III. Private

Community Hospitals Yellow Pages: "Hospitals"*	Wellness Department/ Health Promotions/ Dietary Department/ Nutrition Outpatient Clinic	Nutrition information on lowering high blood cholesterol Nutrition counseling
Health Maintenance Organizations Yellow Pages: "Health Maintenance Organizations"*	Registered Dietitian/ Nutritionist/Health Educator	Nutrition information on lowering high blood cholesterol Nutrition counseling
Registered Dietitians in Private Practice Yellow Pages: "Dietitians" or "Nutritionists"*	Registered Dietitian	Nutrition counseling

* Local Office.

National Cholesterol Education Program Coordinating Committee

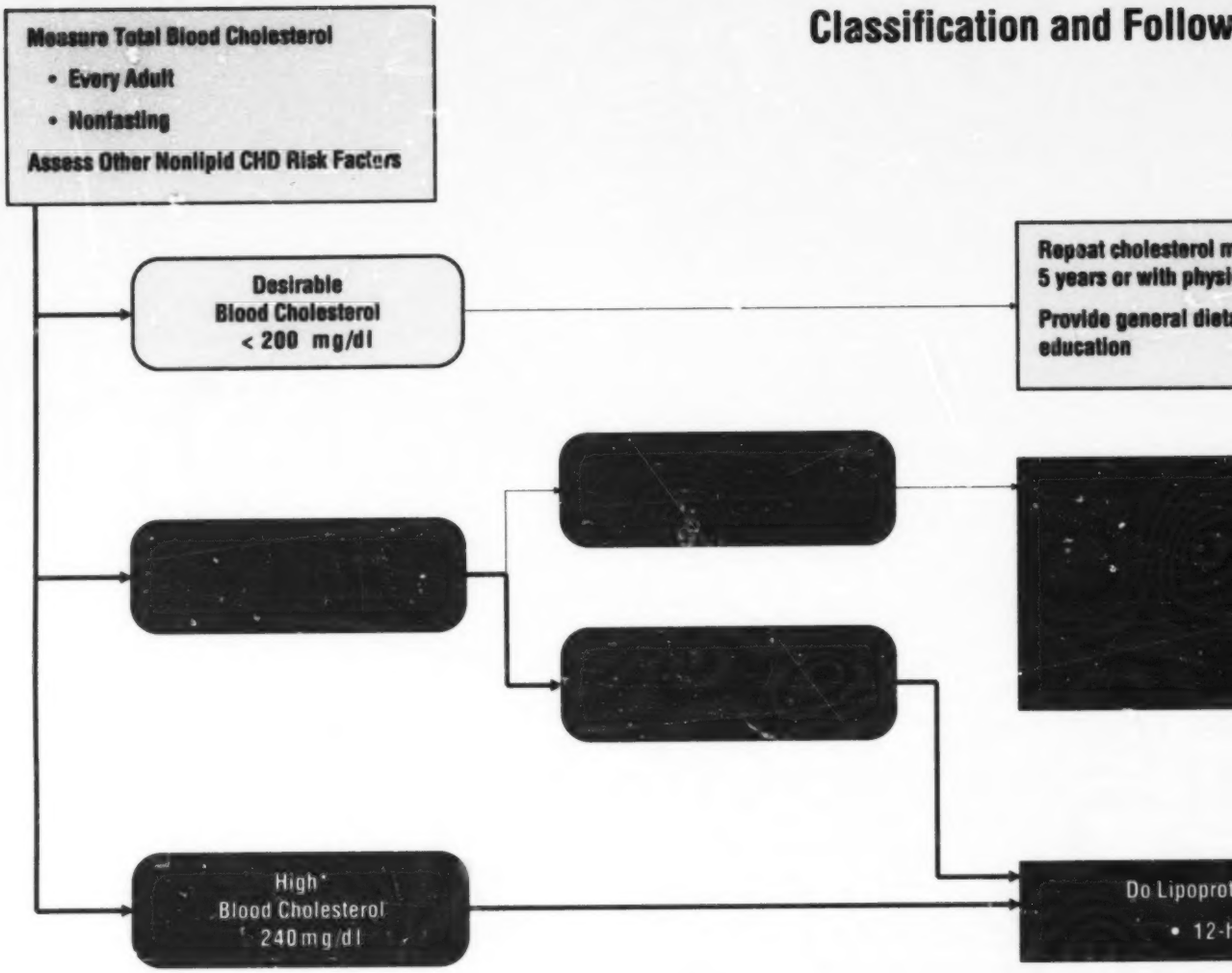
Member Organizations

American Academy of Family Physicians
American Academy of Pediatrics
American Association of Occupational Health Nurses
American College of Cardiology
American College of Physicians
American College of Obstetricians and Gynecologists
American College of Preventive Medicine
American Dietetic Association
American Heart Association
American Hospital Association
American Medical Association
American Nurses Association
American Occupational Medical Association
American Osteopathic Association
American Pharmaceutical Association
American Public Health Association
American Red Cross
Association of Black Cardiologists
Association of Life Insurance Medical Directors of America
Association of State and Territorial Health Officials
Citizens for Public Action on Cholesterol
National Black Nurses' Association, Inc.
National Heart, Lung, and Blood Institute
National Medical Association
Society for Nutrition Education

Liaison Representatives

Ad Hoc Committee on Cardiovascular/Pulmonary Disease Risk Factors in Minority Populations (NHLBI Committee)
Centers for Disease Control
Coordinating Committee for the Community Demonstration Studies
Department of Agriculture
Department of Defense
Food and Drug Administration
Health Resources and Services Administration
National Cancer Institute
National Center for Health Statistics
Office of Disease Prevention and Health Promotion
Veterans Administration

Classification and Follow



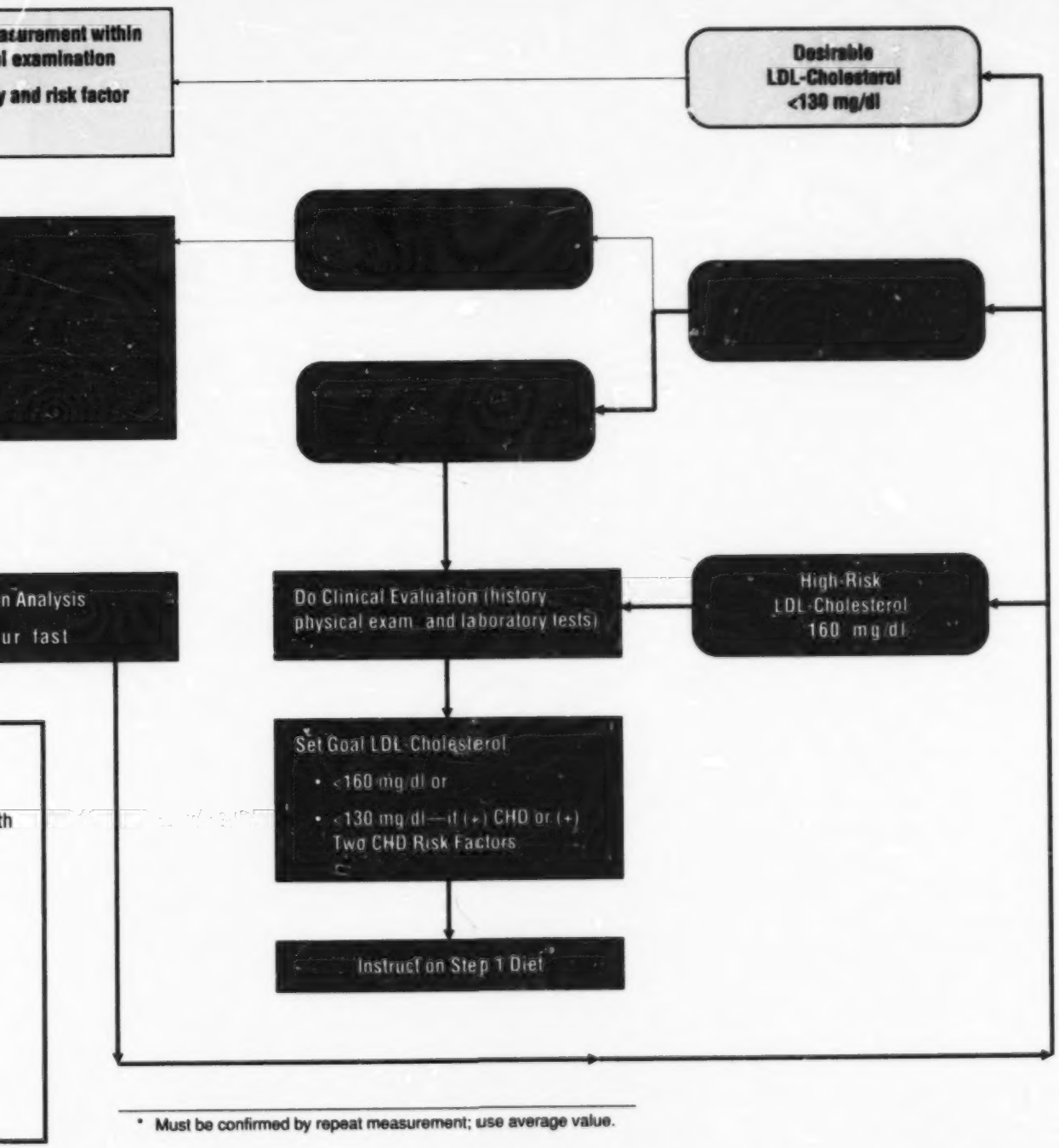
Coronary Heart Disease Risk Factors

- **Male sex**
- **Family history of premature CHD** (definite myocardial infarction or sudden de before age 55 in a parent or sibling)
- **Cigarette smoking** (currently smokes more than 10 cigarettes per day)
- **Hypertension**
- **Low HDL-cholesterol concentration** (below 35 mg/dl confirmed by repeat measurement—not determined at initial screening)
- **Diabetes mellitus**
- **History of definite cerebrovascular or occlusive peripheral vascular diseas**
- **Severe obesity** (≥ 30% overweight)

National Cholesterol Education Program
National Institutes of Health
National Heart, Lung, and Blood Institute
C-200
Bethesda, Maryland 20892

Source: *Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults,*
NIH Publication No. 88-2925,
January 1988

ıp by Total and LDL-Cholesterol Levels



* Must be confirmed by repeat measurement; use average value.

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